RVD2009–05

Re-evaluation Decision

Formetanate Hydrochloride

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Re-evaluation Decision for Formetanate Hydrochloride

After a re-evaluation of the insecticide formetanate hydrochloride, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting continued registration of products containing formetanate hydrochloride for sale and use in Canada.

An evaluation of available scientific information found that under the revised conditions of use, products containing formetanate hydrochloride have value in the food and crop industry and do not present unacceptable risks to human health or the environment. As a condition of the continued registration of formetanate hydrochloride, new risk-reduction measures must be included on the labels of all products. Additional data are being requested.

The regulatory approach for the re-evaluation of formetanate hydrochloride was first presented in Proposed Re-evaluation Decision PRVD2008-26, *Formetanate Hydrochloride*.[1] This Re-evaluation Decision[2] describes this stage of the PMRA's regulatory process for the re-evaluation of formetanate hydrochloride as well as summarizes the Agency's decision and the reasons for it. No comments were received during the consultation process. This decision is consistent with the proposed re-evaluation decision stated in PRVD2008-26, *Formetanate Hydrochloride*. To comply with this decision, registrants of products containing formetanate hydrochloride will be informed of the specific requirements affecting their product registration(s) and of regulatory options available to them.

For more details on the information presented in this Re-evaluation Decision, please refer to the Science Evaluation in the related Proposed Re-evaluation Decision PRVD2008-26, *Formetanate Hydrochloride*.

What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment, will result from use or exposure to the product under its conditions or proposed conditions of registration.[3] The Act also requires that products have value[4] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; (c) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies rigorous, modern hazard and risk assessment methods and policies. These methods consider the unique characteristics of sensitive populations in humans (e.g. children) and organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides.

For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

What Is Formetanate Hydrochloride?

Formetanate hydrochloride is a broad spectrum, Resistance Management Group 1A (carbamate) insecticide that acts as a cholinesterase inhibitor. It works by contact and stomach (ingestion) action. Formetanate hydrochloride is registered in Canada for use on apples, pears, peaches and nectarines to control white apple leafhopper (apples only), European red mites and twospotted spider mites. Aerial application of this active ingredient is not supported by the registrant.

Health Considerations

Can Approved Uses of Formetanate Hydrochloride Affect Human Health?

Additional risk-reduction measures are required on formetanate hydrochloride labels. Formetanate hydrochloride is unlikely to affect your health when used according to the revised label directions.

People could be exposed to formetanate hydrochloride by consuming food and water, when working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the dose levels at which no health effects occur and the dose levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed, when using formetanate hydrochloride products according to label directions.

Acute overexposure to formetanate hydrochloride can inhibit cholinesterase, an enzyme necessary for normal functioning of the nervous system. This can produce a variety of symptoms in animals and humans including tremors, body stiffening, lacrimation, salivation, convulsions, unsteady gait, vomiting, laboured respiration, decreased motor activity, lethargy and muscle weakness. With formetanate hydrochloride, cholinesterase

inhibition can occur rather rapidly with exposure (within minutes), but animals and humans rapidly recover along with any of the aforementioned symptoms. Young animals in toxicity studies were more sensitive than the adults following oral exposures, with more pronounced effects on cholinesterase observed. Inhaling formetanate hydrochloride resulted in low to moderate acute toxicity, depending on the duration of dosing. Local effects of acute dermal exposure were minimal; however, the potential for skin sensitization does exist. Contact with the eye may also cause moderate eye irritation. To prevent overexposure, the label directions must be followed.

Additional findings in repeat-dose animal studies including those in pregnant animals consisted of decreases in body-weight gain and food consumption. There were a small number of positive genotoxicity results noted, however, the findings were equivocal at best; overall there was no great concern with respect to genotoxicity, with most studies showing negative results. Likewise, while higher dose levels could have been employed in certain cancer studies, there was no concern identified with respect to carcinogenicity. A cancer risk assessment was not required. The described effects would likely not occur when formetanate hydrochloride products are used according to the label directions.

As there were some risks of concern based on current uses of formetanate hydrochloride, additional protective measures are required on product labels to further reduce the level of human exposure to formetanate hydrochloride.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern.

There are currently no residential uses of formetanate hydrochloride registered. Given homeowners would not be applying the product, a risk assessment for this scenario was not conducted.

Occupational Risks From Handling Formetanate Hydrochloride

Occupational risks are not of concern provided additional risk-reduction measures are observed.

Risk estimates associated with applying, mixing and loading activities for the global label uses are acceptable, provided engineering controls and/or personal protective equipment are used. These measures are needed to minimize potential exposure and protect worker's health.

Postapplication risks are not of concern to workers provided additional risk-reduction measures are observed.

Postapplication occupational risk assessments consider exposures to workers entering treated sites in agriculture. When the required mitigation measures are considered, postapplication risks are not of concern.

Residues in Water and Food

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that over a lifetime, is believed to have no significant harmful effects.

Human exposure to formetanate hydrochloride was estimated from residues in treated crops and drinking water, including the most highly exposed subpopulation (e.g. infants less than one year old). Two approaches were used to assess dietary risk. In the first approach, limited field trial data were used to estimate residues in food. Given there were limitations in the field trial data, a second approach was used in which monitoring data of residues in foods available to Canadian consumers were used. Using the former approach, aggregate exposure (i.e. to formetanate hydrochloride from food and drinking water) represents less than 75% of the acute reference dose and less than 2% of the chronic reference dose. When using the latter approach, aggregate exposure is less than 96% of the acute reference dose and less than 0.3% of the chronic reference dose for all subpopulations, with the exception of infants. Aggregate exposure for infants is greater than 400% of the acute reference dose, indicating that risk mitigation for dietary exposure is required for this subpopulation.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for the *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

MRLs for formetanate hydrochloride are currently specified for apples, pears, peaches, nectarines, citrus fruits and plums. Where no specific MRL has been established, a default MRL of 0.1 ppm applies which means that pesticide residues in a food commodity must not exceed 0.1 ppm. Given changes in the use pattern of formetanate hydrochloride and as a result of the dietary risk assessment, the MRLs for formetanate hydrochloride need to be revised.

Environmental Considerations

What Happens When Formetanate Hydrochloride is Introduced Into the Environment?

Formetanate hydrochloride poses a potential risk to beneficial predatory terrestrial invertebrates and aquatic invertebrates; therefore, additional risk reduction measures need to be observed.

Formetanate hydrochloride is very soluble in water and is very susceptible to hydrolytic transformation and phototransformation, in both soil and water at neutral and basic pH conditions. Acidic conditions result in slower transformation of parent formetanate hydrochloride. Soil biotransformation also takes place quickly so formetanate hydrochloride is unlikely to persist in soil or water after application. There were no major transformation products formed in any of these processes. Formetanate hydrochloride is considered to have moderate mobility in most soils; however, modelling predicts that only low concentrations will reach surface water and no residues will be found in ground water.

When formetanate hydrochloride is used for insect control in crops, there is a potential that nontarget species on land and in water may be exposed to the chemical as a result of spray drift or runoff. Some species are sensitive to the chemical and would be adversely affected. Formetanate hydrochloride presents a risk to aquatic organisms like freshwater invertebrates and terrestrial beneficial predatory insects and mites. To minimize potential exposure to these biota, strips of land between the agricultural field and the nontarget areas will be left unsprayed. The width of these buffer zones will be specified on the product label. An appropriate label statement describing the risk to beneficial predatory terrestrial insects is required.

Birds and small mammals could be at risk from the use of formetanate hydrochloride, however, the risk assessment is considered to be overly conservative due to the fact that formetanate hydrochloride has rapid photolytic and hydrolytic transformation. These factors indicate that it is unlikely that these biota will be exposed to formetanate hydrochloride at sufficient concentrations to result in risk. Fish and marine invertebrates are at negligible risk from use of formetanate hydrochloride.

Modelling predicts that formetanate hydrochloride will not be present in runoff or in surface waters due to drift, at concentrations that present a risk to aquatic biota.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of formetanate hydrochloride, the PMRA is requiring further risk-reduction measures for product labels.

Additional Key Risk-Reduction Measures

Human Health

- Limit application to once per season, reduce rate of application and limit timing of application to early season, to minimize residues on treated food crops.
- Require additional protective equipment and/or engineering controls, limit application to once per season, reduce rate of application and remove aerial application to protect mixer/loader/applicators.
- Limit application to once per season, reduce rate of application, limit timing of application to early season and establish restricted-entry intervals to protect workers entering treated sites.

Environment

- Adding precautionary label statements and directions for use as well as buffer zones to protect non-target terrestrial and aquatic plants.
- Adding statements cautioning use on sites with characteristics that may enhance runoff when heavy rain is forecasted to reduce the potential runoff of formetanate hydrochloride to adjacent aquatic habitats.

Appendix I lists all the required label amendments.

What Additional Scientific Information is Being Requested?

Human Health

Given the changes in the use pattern of formetanate hydrochloride and as a result of the dietary risk assessment, the MRLs for formetanate hydrochloride must be reviewed and revised.

- To assess and revise the MRLs of formetanate hydrochloride, all residue data including field trials submitted to the United States Environmental Protection Agency (USEPA) must be submitted within one year of the re-evaluation decision document. This includes but is not limited to, all field trials in stone fruit, pome fruit, citrus fruit, plant and livestock metabolism studies, food processing studies, analytical methodology studies, and storage stability studies. To facilitate the PMRA review, it is highly recommended that USEPA reviews of these studies be submitted also.

- In addition, all residue data including field trials to be submitted to the USEPA as a result of their evaluation as outlined in the document: *Formetanate Hydrochloride HED Revised Chemistry Chapter of the RED: Summary of Analytical Chemistry and Residue Data (Phase 4),* must be submitted within one year of the final re-evaluation decision. This includes but is not limited to, all field trials in stone fruit, pome fruit, citrus fruit and clarifications for plant metabolism studies.

Other Information

For formetanate hydrochloride, the summary of assessments found in PRVD2008-26 serves as an evaluation report. A list of references considered by the PMRA in support of the registration decision are found in this Re-evaluation Decision (Appendix II). The relevant test data on which the decision is based are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail pmra_infoserv@hc-sc.gc.ca.

Any person may file a notice of objection[5] regarding this decision on formetanate hydrochloride within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website, www.hc-sc.gc.ca/cps-spc/pest/protect-proteger/publi-regist/index-eng.php#rrd or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail pmra_infoserv@hc-sc.gc.ca.

Once all carbamate pesticides have been re-evaluated, a cumulative risk assessment will be conducted, which will consider potential exposure to all chemicals causing toxicity in the same manner. The results of the cumulative risk assessment may affect any previous re-evaluation decision.

[5]As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Label Amendments for Products Containing Formetanate Hydrochloride

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the label statements below.

The Canadian restricted end-use product label for Registration Number 11144 must be amended to include the following changes and statements, to further protect human health and the environment.

GENERAL LIMITATIONS

RESTRICTED USES:

The following text in Registration Number 11144:

> **RATE:** 250–500 g per 100 litres of dilute spray (4000–5000L of water per ha) or AT LEAST 1.1 kg per hectare.

must be amended to:

> **RATE:** 250–500 g per 1000 litres of dilute spray (4000–5000L of water per ha) or AT LEAST 1.1 kg per hectare. DO NOT apply more than once per growing season. Apply at a maximum rate of 1.40 kg product/ha equivalent to 1.29 kg a.i./ha for all crops.

The current PHIs must be removed.

The following text in Registration Number 11144:

> Apples and Pears: Apply when mites or insects are first noticed and repeat as needed. Do not apply later than 1 day before harvest on apple and pear. To avoid excessive residue, do not apply more than 4.48 kg per hectare after Calyx.
>
> Peaches and Nectarines: Apply when a threshold of 5–10 active mites per leaf is reached (mid-July to early August). The majority of the mite population should be in the young nymphal stage. Do not apply later than 21 days before harvest. Do not apply more than once per year.

must be amended to:

> Pome fruits (apples and pears): Pesticide products containing the active ingredient formetanate hydrochloride should not be applied after petal fall. Late season applications are not permitted. Apply when mites or insects are first noticed.
>
> Peaches and nectarines: Pesticide products containing the active ingredient formetanate hydrochloride should not be applied after petal fall. Late season applications are not permitted. The majority of the mite population should be in the young nymphal stage.

All instructions related to aerial applications must be removed from the current label.

TOXICOLOGICAL INFORMATION:

Formetanate hydrochloride is a carbamate which is a cholinesterase inhibitor. Typical symptoms of overexposure to cholinesterase inhibitors include malaise, muscle weakness, dizziness and sweating. Headache, salivation, nausea, vomiting, abdominal pain and diarrhea are often prominent. A life-threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). However, if a blood sample is taken several hours after exposure, it is unlikely that blood cholinesterase activities will be depressed, due to rapid reactivation of cholinesterase. Atropine, only by injection, is the preferable antidote. Do not use pralidoxime. In cases of severe acute poisoning use antidotes immediately after establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician.

PRECAUTIONARY STATEMENTS

PROTECTIVE CLOTHING AND EQUIPMENT:

> Respirators are required for all mixer/loaders.
>
> During airblast application, use a closed cab that provides both a physical barrier and respiratory protection (i.e. dust/mist filtering and/or vapour/gas purification system). During application wear long-sleeved shirt, long pants and chemical-resistant gloves. Keep the following personal protective equipment immediately available for use in case of emergency (i.e. a broken package, spill or equipment breakdown): chemical-resistant coveralls, chemical-resistant gloves, chemical-resistant headgear and a respirator.

If a closed cab is not used, wear long pants, long-sleeved shirt, shoes plus socks, chemical-resistant gloves, chemical-resistant headgear and chemical-resistant coveralls and NIOSH approved respiratory protection. Chemical-resistant headgear includes So'westers or large brimmed waterproof hats and hoods with sufficient neck protection. Avoid touching face or other unprotected parts of the body during application.

Label language should be clarified to indicate directions for water-soluble packaging.

USE PRECAUTIONS:

For commercial orchard use only. Do not use in residential areas such as parks, schools or backyards.

Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature, application equipment and sprayer settings.

RESTRICTED-ENTRY INTERVAL:

The following restricted-entry intervals must be observed by workers re-entering the treated areas for these crops.

Crop	Activity	REI (day)
Apples Pears Peaches Nectarines	Thinning	19
	Harvesting, propping, pruning, training	14
	Weeding, irrigating, scouting	12

ENVIRONMENTAL HAZARDS:

- **TOXIC** to aquatic organisms. Observe buffer zones specified under **DIRECTIONS FOR USE. TOXIC** to birds
- **TOXIC** to small wild mammals
- **TOXIC** to certain beneficial insects. Minimize spray drift to reduce harmful effects on beneficial insects in habitats next to the application site, such as hedgerows and woodland
- To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to: heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. soils that are compacted or fine textured such as clay).
- Avoid application of this product when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced, by including a vegetative strip between the treated area and the edge of the water body.

DIRECTIONS FOR USE

- **DO NOT** apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, coulees, prairie potholes, creeks, marshes, streams, reservoirs, ditches and wetlands), estuaries or marine habitats.
- **DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
- **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty.
- **R.E. Airblast or Mist blower application:**
  DO NOT direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site, as measured outside of the treatment area on the upwind side.
- **DO NOT** apply this product by air.
- The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats, (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	**Crop**	**Buffer Zones (metres) Required for the Protection of Freshwater Habitat of Depths:**	
		Less than 1 m	**Greater than 1 m**
Airblast (early and late growth stages)	Apple, Pear, Peach, Nectarines	3	1

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

References

A. Studies/Information Provided by the Applicant/Registrant (Unpublished)

Chemistry

Reference 2003, Manufacturing Summary.
PMRA Document Number 1452034

Reference 1982, Formetanate Hydrochloride Technical Description Of Raw Materials And Manufacturing DCE-free Process.
PMRA Document Number 1452035

Reference 1995, Discussion Of The Formation of Impurities In The Technical Grade Substance.
PMRA Document Number 1452036

Reference 1995, Formetanate Hydrochloride, Lack Of Toxicological Significance Of Two New Impurities In Formetanate Hydrochloride Resulting From Synthesis Using The DCE-Free Process.
PMRA Document Number (1452037

Reference 1996, Hoe 132807, Formetanate Hydrochloride Analytical Profile Of Five Typical Production Batches.
PMRA Document Number 1452015

Reference 1996, Hoe 132807, Comparison Of DCE-Containing And DCE-Free Production Batches.
PMRA Document Number 1452041

Toxicology

Reference (1991) Technical Formetanate Hydrochloride: Mouse Micronucleus Test. Unpublished study prepared by Huntingdon Research Centre Ltd. Feb. 12th, 1991.
PMRA Document Number 1144890

Reference (1969) Effects of Formetanate on Cholinesterase activity in Dog Plasma after Oral Administration of the Compound. Unpublished study prepared by Schering AG, June 4th, 1969.
PMRA Document Number 1204479

Reference (1972) Knowles C. O., Ahmad S. "Mode of Action Studies with Formetanate and Formparanate Acaricides." Pesticide Biochemistry and Physiology 1, (1972) 445-452.
PMRA Document Number 1204480

Reference (1985) Technical Formetanate Hydrochloride: Effect on whole blood cholinesterase activity in male rats. Unpublished study prepared by FBC Limited Chesterford Park Research Station. March 7th, 1985.
PMRA Document Number 1204481

Reference (1982) Waters M. D., et al. "Study of Pesticide Genotoxicity." Basic Life Science 21, (1982) 275-326.
PMRA Document Number 1204667

Reference (1985) Klopman G., et al "Structure-genotoxic activity relationships of pesticides: comparison of the results from several short-term assays" Mutation Research 147, (1985) 343-356.
PMRA Document Number 1204668

Reference (1986) Garrett N. E., et al "Evaluation of the genetic activity profiles of 65 pesticides." Mutation Research 168, (1986) 301-325.
PMRA Document Number 1204669

Reference (1985) Technical Formetanate Hydrochloride: Metaphase Chromosome Analysis of Human Lymphocytes Cultured In Vitro. Unpublished study prepared by Huntingdon Research Centre. April 30th, 1985.
PMRA Document Number 1204670

Reference (1985) Technical Formetanate Hydrochloride: Mouse Lymphoma Mutation Assay. Unpublished study prepared by Huntingdon Research Centre. February 18th, 1985.
PMRA Document Number 1204671

Reference (1988) TECHNICAL FORMETANATE HYDROCHLORIDE: An evaluation of dietary oncogenic potential in. the mouse. Unpublished study prepared by Schering Agrochemicals Limited. June 24th, 1988.
PMRA Document Number 1218456

Reference (1988) TECHNICAL FORMETANATE HYDROCHLORIDE: An evaluation of dietary oncogenic and chronic toxicity potential in the rat. Unpublished study prepared by Schering Agrochemicals Limited. May 13th, 1988.
PMRA Document Number 1218458

Reference (1988) TECHNICAL FORMETANATE HYDROCHLORIDE: An evaluation of dietary oncogenic and chronic toxicity potential in the rat. Unpublished study prepared by Schering Agrochemicals Limited. May 13th, 1988.
PMRA Document Number 1218467

Reference (1987) TECHNICAL FORMETANATE HYDROCHLORIDE: The Reproductive Performance of Rata Treated Continuously Through Two Successive Generations. Unpublished study prepared by Life Science Research Limited. September 28th, 1987.
PMRA Document Number 1218478
Reference (2005) Oral (Gavage) Acute Relative Sensitivity Study of Formetanate HC1 in Neonatal and Adult Rats. Unpublished study prepared by Charles River Laboratories. August 4th, 2005.
PMRA Document Number 1302275

Reference (2000) Rat Dermal Time to Peak Effect Study for Acetyl Cholinesterase Inhibition Formetanate Hydrochloride. Unpublished study prepared by Sequani Limited. October 10th, 2000.
PMRA Document Number 1459579

Reference (1999) RAT 21-Day Dermal Toxicity Study Formetanate Hydrochloride. Unpublished study prepared by Quintiles Toxicology/Pathology Services, Quintiles England Limited . October 10th, 2000.
PMRA Document Number 1459580

Reference (1967) Report to Morton Chemical Company Acute Toxicity Studies on EP-332 HC1, Technical., A5341.
PMRA Document Number 1584601

Reference (1967) Report to Morton Chemical Company Acute Oral Toxicity of EP-332 HC1 to Mongrel Dog., J5395.
PMRA Document Number 1584602

Reference (1967) Report to Morton Chemical Company Acute Dust Inhalation Toxicity of EP-332 HC1, Technical., N5342.
PMRA Document Number 1584603

Reference (1968) Report to Morton Chemical Company Acute Aerosol Inhalation Toxicity on EP-332 HC1 Technical., N6224.
PMRA Document Number 1584604

Reference (1970) Sen Gupta, A.K. and C.O. Knowles, 1970, Fate of Formetanate-14C Acaricide in the Rat Journal of Economic Entomology 10-14 Vol. 63 No. 1.
PMRA Document Number 1584605

Reference (1970) Report to NOR-AM Agricultural Products Acute Oral Toxicity Study on Formetanate Hydrochloride and Six Metabolites of Formetanate Hydrochloride in Male and Female Albino Rats., A8219.
PMRA Document Number 1584606

Residue Chemistry

Reference Nelson, R.D. 1979. Residue data to support minor use registration on strawberries (Carzol SP). Driscoll Strawberry Association, Watsonville, CA. Unpublished.
PMRA Document Number 1137223

Reference Moede, J. 1989. R169 Formetanate HCl: residues of formetanate HCl and major metabolites in strawberries following application of Carzol 92SP in the USA 1988. Schering AG, Berlin, Germany. Unpublished.
PMRA Document Number 1137224

Reference Wrede-Rucker, A. 1990. R181 Formetanate HCl: residues of formetanate HCl and major metabolites in strawberries following application of a SP-formulation in Canada 1989 (Carzol SP). Schering AG, Berlin, Germany. Unpublished.
PMRA Document Number 1137225

Reference Jenny, N.A. (compiled with a summary by J.J. Vukich). 1989. Residue data for the use of Carzol SP on strawberries. NOR-AM Chemical Company, Wilmington, Delaware. Unpublished.
PMRA Document Number 1230496

Reference Scheuermann, H.J. 1987. R155 Formetanate HCl GLC method of analysis for major formetanate derived residues in nectarines. Schering AG, Berlin, Germany. Unpublished.
PMRA Document Number 1144901

Reference Nelson, R.D. 1979. Residue Report, Carzol SP on strawberries in loam soil. Driscoll Strawberry Association, Watsonville, CA. Unpublished.
PMRA Document Number 1157490

Reference No author. 1974. Residue Report, Carzol SP on strawberries. Nelson, Watsonville, CA. Unpublished.
PMRA Document Number 1157491

Reference Moede, J. 1989. R169 Formetanate HCl: Residues of formetanate HCl and major metabolites in strawberries following application of Carzol 92 SP in the USA 1988. Schering AG, Berlin, Germany. Unpublished.
PMRA Document Number 1157492

Reference Wrede-Rucker, A. 1990. R181 Formetanate HCl: residues of formetanate HCl and major metabolites in strawberries following application of a SP-formulation in Canada 1989 (Carzol SP). Schering AG, Berlin, Germany. Unpublished.
PMRA Document Number 1157493

Reference Paik, Y.J.. 2000. Residue data submitted in support of minor use of Carzol to control European red mite on grapes. Laboratory Services Division, University of Guelph, Guelph, ON. Unpublished.
PMRA Document Number 1197170

Occupational and Residential Exposure

Reference AgrEvo, October 1996. Dissipation of Foliar Dislodgeable Residues of Formetanate Hydrochloride Following Application of CARZOL® SP to Apples and Citrus, USA, 1995: Pikeville, NC. ID U044/R742.

B. Additional Information Considered for the Formetanate Hydrochloride Re-evaluation (Published Information)

Toxicology

Reference (2002) California Environmental Protection Agency, 2002, SUMMARY OF TOXICOLOGY DATA FORMETANATE HCL, 3/14/00 (Revised date 8/29/02) - www.cdpr.ca.gov/docs/risk/toxsums/pdfs/111.pdf.

Reference (2003) USEPA Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision Document Date completed: April 4, 2003.

Reference (1993) Formetanate - Evaluation of Mammalian Toxicology and Toxicokinetic/ Metabolism Data. October 1993.

Residue Chemistry

Reference U.S. EPA. March 27, 2003. Revised Chemistry Chapter of the RED: Summary of Analytical Chemistry and Data.

Reference U.S. EPA. April 28, 2003. Formetanate Hydrochloride, Acute (Probabilistic) and Chronic Dietary Exposure Assessment for the Reregistration Eligibility Decision.

Reference U.S. EPA. June 4, 2003. HED Revised Revised Risk Assessment for Formetanate Hydrochloride.

Reference U.S. EPA. December 14, 2005. Formetanate Hydrochloride HED Revised Chemistry Chapter of the RED: Summary of Analytical Chemistry and Residue Data (Phase 4).

Reference U.S. EPA. December 16, 2005. Formetanate Hydrochloride: Revised Acute Probabilistic and Chronic Dietary Exposure Assessments for the Reregistration Eligibility Decision.

Reference U.S. EPA. December 23, 2005. HED Revised Risk Assessment for Formetanate Hydrochloride (097301) (Phase 4), D323945.

Reference U.S. EPA. March, 2006. Interim Reregistration Eligibility Decision for Formetanate Hydrochloride. EPA 738-R-06-015.

Reference U.S. EPA. June 8, 2006. Memorandum. Subject: Formetanate Hydrochloride. Addendum to the HED Revised Risk Assessment for Formetanate Hydrochloride dated December 23, 2005.

Reference U.S. EPA. April 17, 2007. Revised Formetanate HCl IRED.

Reference U.S. EPA. September 24, 2007. Memorandum. Completion of the Tolerance Reassessment and Final Reregistration Eligibility Decisions for N-methyl Carbamate Pesticides.

Occupational and Residential Exposure

Reference US EPA. April 2007. Revised Reregistration Eligibility Decisions Document for Formetanate Hydrochloride. US EPA Office of Prevention, Pesticides and Toxic Substances: Washington, DC.

Environment

Reference Hardman, J.M., J.L., Franklin, D.L. Moreau and N.J. Bostanian. 2003. An index for selective toxicity of miticides to phytophagous mites and their predators based on orchard trials. Pest Manag. Sci. 59:1321-1332.

Reference Hassan, S.A., R. Albert, F. Bigler, P. Blaisinger et al. 1987. Results of the Third Joint Pesticide Testing Programme by the IOBC/WPRS-Wworking Group "Pesticides and Beneficial Organisms". Z. Angew. Entomol. 103:92-107.

Reference MSDS 2001. Material Safety and Data Sheet Carzol SP.

Reference NAWQA (2006) The USGS National Water Quality Assessment Program (NAWQA) summary data for pesticide occurrence and concentrations in ground water from agricultural and urban wells, as well as 31 integrator sites on large rivers and streams.. Downloaded 2006. http://water.usgs.gov/nawqa/

Reference National Contaminant Occurrence Database (NCOD). www.epa.gov/safewater/data/ncod.html.

Reference Niemann RA. 1993. Determination of formetanate hydrochloride in selected fruits by coupled-column cation exchange liquid chromatography. J AOAC Int. 76(6):1362-1368.

Reference U.S. EPA R.E.D.. 1997. EFED Science Chapter for the Formetanate Hydrochloride Reregistration Eligibility Document (Chemical #097301, DP Barcodes D232763, D232766). Office of Prevention, Pesticides and Toxic Substances. August 29, 1997. 61 pp.

Reference U.S. EPA. 1999. HED Preliminary Risk Assessment for Formetanate Hydrochloride (097301), Case 0091, DP Barcode D233099. Health Effects Division, Office of Pesticide Programs. 84 pp.

Reference U.S. EPA. 2003. Formetanate Hydrochloride. Crop Field Trials - Pears, Apples, Peaches. OPP Official Record, HED, Science Data Reviews, EPA Series 361. MRID# 45485001.

Reference U.S. EPA R.E.D. 2003a. Formetanate Hydrochloride HED Revised Chemistry Chapter of the R.E.D.: Summary of Analytical Chemistry and Residue Data. Office of Prevention, Pesticides and Toxic Substances. March 27, 2003. 14 pp.

Reference U.S. EPA R.E.D.. 2003b. EFED Science Chapter for the Formetanate Hydrochloride Reregistration Eligibility Document. Office of Prevention, Pesticides and Toxic Substances. October 22, 2003. 72 pp.

Reference U.S. EPA R.E.D.. 2003c. Formetanate PC Code: 097301 Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision Document. Health Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency.

Use Analysis

Reference Cranshaw, W.S. 2003. Insect Control Soaps and Detergents. Colorado State University Cooperative Extension - Horticulture Factsheet 5.547 Colorado State University Cooperative Extension web page: www.ext.colostate.edu/pubs/insect/05547.html Site accessed April 12, 2005.

Reference Smith, R., Chancy, B. and A. Antonelli. 2003. Guidelines for Insecticidal Soap. Washington State University. Washington State University Extension: Site accessed April 12, 2005

C. Additional Information Considered for the Formetanate Hydrochloride Re-evaluation (Unpublished Information)

Toxicology

Reference (1978) PMRA Review. May 18th, 1978.
PMRA Document Number 1652620

Occupational and Residential Exposure

Reference USEPA. July 1997. Review of the AgrEvo study entitled "Dissipation of Foliar Dislodgeable Residues of Formetanate Hydrochloride Following Application of Carzol® SP to Apples and Citrus, USA, 1995."
PMRA Document Number 1048876